International Journal of Advances in Medicine
Kaur R et al. Int J Adv Med. 2020 Dec;7(12):1789-1794
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20204999

Original Research Article

Study of demographic, hematological profile and risk stratification in chronic myeloid leukemia patients, in and around North-West Punjab, India

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Received: 21 October 2020
Revised: 08 November 2020
Accepted: 09 November 2020

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ABSTRACT

Background: Chronic myeloid leukemia (CML) is a hematopoietic stem cell disorder with cytogenic profile and tyrosine kinase inhibitors used as its therapy. Objective of the present study was to determine the demographic, haematological profile and to characterize them in low and high-risk group on presentation with European treatment and outcome study score (EUTOS) in CML patients in and around North-West Punjab, India.
Methods: Diagnosed cases of CML were taken. Investigations were done. Molecular and cytogenetic studies were also done whenever required and with EUTOS patients were stratified and then treatment was individualized.
Results: Total 100 patients were enrolled. The mean age of presentation of CML was 44.7 years with M:F ratio was 1:1. 20% cases were of Hindu religion and 80% cases were Sikh by religion. 68% cases from rural area and 32% cases were from urban area. 92 patients were in chronic phase, 5 patients in accelerated phase, and 3 patients were found in blast crisis phase. Out of total 100 cases, 32% cases were of high-risk group and 68% cases were of low-risk group on presentation according to EUTOS.
Conclusions: Most CML patients in north west Punjab are young (31-40 years) with male: female ratio is 1:1. Majority of them were Sikh by religion and from rural area. Most of them presented in Chronic phase of the disease and with low-risk strata according to EUTOS. Conclusion is that most patients presents in early phase of disease, with anaemia, leucocytosis or splenomegaly.

Keywords: Accelerated phase, Blast crisis, Chronic phase, Chronic myeloid leukaemia, European treatment and outcome study score

INTRODUCTION

Chronic myelogenous leukaemia (CML) is a myeloproliferative disorder, characterized by clonal expansion of abnormal pluripotent haemopoietic stem cell, arising from reciprocal translocation of genetic material between long arms of chromosome 9 and 22.[1] The resulting BCR-ABL fusion gene is derived from translocation of *abl* gene on chromosome 9, which becomes juxtaposed to bcr gene on chromosome 22.[2] The BCR-ABL oncogene results in constitutive expression of an oncoprotein (p210) with tyrosine kinase activity, which causes activation of anti-apoptotic pathways and unregulated proliferation of stem cells resulting in expansion of myeloid cell mass.3 The disease undergoes clonal evolution from relatively stable chronic phase to an accelerated phase lasting for 4-6 months, and finally

culminating into myeloid or lymphoid blast crisis.4 The annual incidence of chronic myeloid leukaemia in India was originally reported to be 0.8 to 2.2 per 1,00,000 population.[5] There are no familial associations in chronic myeloid leukaemia. The introduction of an inhibitor targeted at the BCR-ABL tyrosine kinase (imatinib) has fundamentally changed treatment of CML.[6] BCR-ABL expression can be reduced by imatinib to very low or nondetectable levels in the majority of patients.[7]

Objectives

Objective were to study demographic and hematological profile of chronic myeloid leukemia patients and to characterize chronic myeloid leukemia patients in low and high-risk group with European treatment and outcome study score (EUTOS).

METHODS

This study was conducted at Department of Medicine and Oncology at Sri guru ram das institute of medical sciences and research, Amritsar, Punjab. All diagnosed cases of chronic myeloid leukaemia were taken into study from June 2019 to June 2020 coming to our tertiary care hospital. The study was approved by the Ethical Committee of the Institute. Detailed history and examination were done with informed consent. Investigations such as complete blood count including haemoglobin level, platelet count, total and differential leucocyte count, general blood picture, and bone marrow aspiration/biopsy were done. Molecular studies such as RT–PCR for BCR-ABL fusion and cytogenetic studies for Philadelphia chromosome were also done whenever required.

Inclusion criteria

Diagnosed patients of chronic myeloid leukemia irrespective to the stage of the disease.

Diagnostic criteria

Following diagnostic tools was used for final diagnosis. 1) Clinical presentation: - fatigue, fever, malaise, weight loss, mass in abdomen, abdominal fullness 2) blood investigation: leucocytosis ranging from 10–500×109/l, the peripheral blood differential shows left-shifted hematopoiesis 3) ultrasound abdomen 4) bone marrow aspiration/biopsy: the bone marrow is hypercellular with marked myeloid hyperplasia, high myeloid-to-erythroid ratio of 15-20:1, marrow blasts varies from 5% to >20% according to the phase of the disease 5) BCR-ABL by RT-PCR quantitative assay test.

Data thus obtained were analysed statistically. The data were presented by mean±standard deviation for continuous variables and frequencies with their respective percentages were given for categorical variables. Correlation coefficient was used to measure the degree of association between two variables. A p value <0.05 was considered as statistically significant.

Study design

It is an observational study.

RESULTS

In total, 100 patients presented with chronic myeloproliferative disorders in which all the patient were diagnosed with CML. The mean age was 44.7, the patients were in the age range of 16-85 years. Overall, most common age group affected were between 31 to 40 year. About 50 (50%) were male and 50 (50%) were female with M:F ratio of 1:1.

Total 20% were of Hindu religion and 80% were Sikh by religion. 68% were from rural area and 32% were from urban area. 92 patients (92%) were in CML-chronic phase (CP), 5 patients (5%) in CML-accelerated phase (AP) phase, and 3 patients (3%) were found in CML-blast crisis (BC) phase.

Table 1: Spleen size and different phase of disease.

		Phase			Total
		Accelerated phase	Blast crisis	Chronic Phase	
Spleen size	Normal	2	2	32	36
		5.6%	5.6%	88.9%	100.0%
	Mild	1	0	25	26
		3.8%	0.0%	96.2%	100.0%
	Moderate	2	1	13	16
		12.5%	6.3%	81.3%	100.0%
	Massive	0	0	22	22
		0.0%	0.0%	100.0%	100.0%
Total		5	3	92	100
		5.0%	3.0%	92.0%	100.0%
P value		0.399 (NS)			

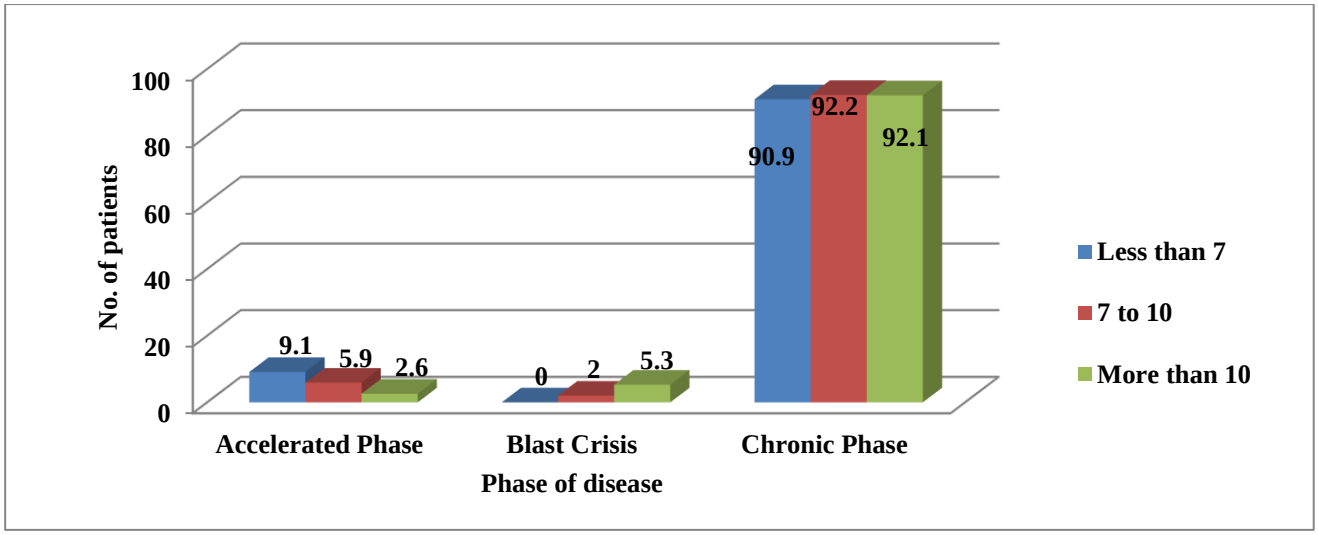

Figure 1: Hemoglobin levels and different phases of disease.

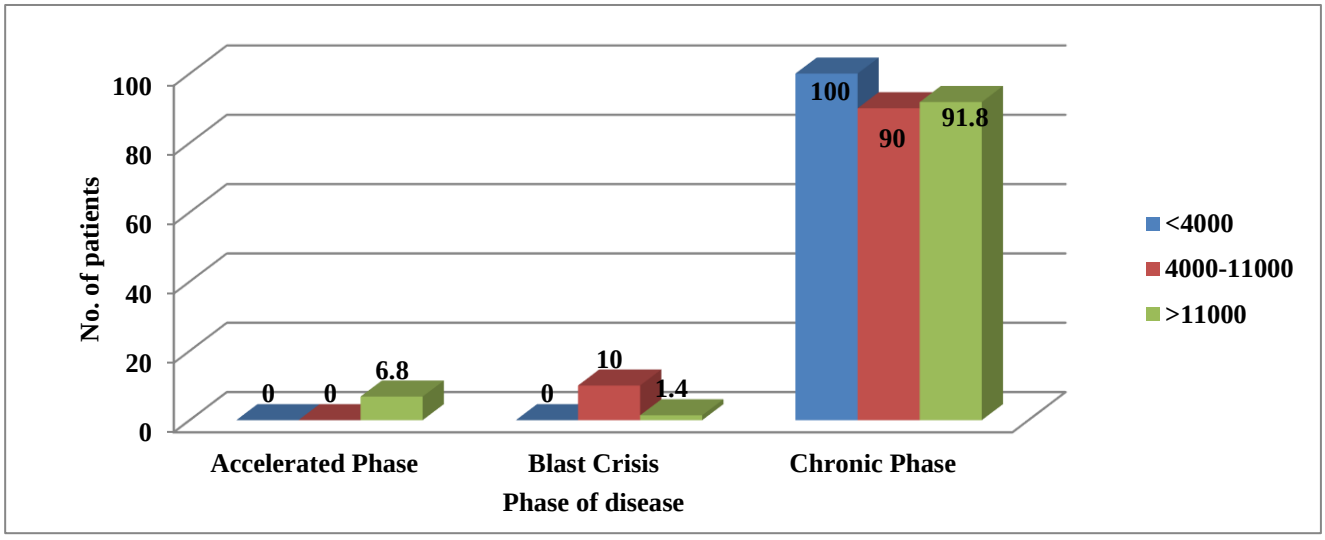

Figure 2: Leucocyte counts and different phases of disease.

Out of total 100, 36 (36%) cases had normal spleen size, 26 (26%) cases had mild splenomegaly, 16 (16%) cases had moderate splenomegaly, and 22 (22%) cases had massive splenomegaly.

In Accelerated phase 2 (40%) cases had normal spleen size, 1 (20%) case had mild splenomegaly and 2 (40%) cases had moderate splenomegaly whereas in blast crises phase, 2 (66.7%) cases had normal spleen size and 1 (33.3%) case had moderate splenomegaly and in chronic phase, 32 (34.8%) cases had normal spleen size, 25 (27.2%) cases had mild splenomegaly, 13 (14.1%) cases had moderate splenomegaly and 22 (23.9%) cases had massive splenomegaly (Table 1).

In CP, 35 (38%) cases presented with haemoglobin levels >10 mg/dl, 47 (51.1%) cases presented with moderate anaemia, whereas only 10 (10.9%) cases presented with severe anaemia. In AP, 1 (20%) case presented with haemoglobin levels >10 mg/dl, 3 (60%) cases presented with moderate anaemia, whereas only 1 (20%) case presented with severe anaemia. In BC phase, 2 (66.7%) cases presented with haemoglobin levels >10 mg/dl, 1 (33.3%) case presented with moderate anaemia, and none of the case had severe anaemia (Figure 1).

Normal leucocyte counts: (4000-11000)/µl, leucopenia: <4000/µl, leucocytosis: >11000/µl.

Out of 100, 20 cases had normal leucocyte count, 6 cases had leucopenia and 74 cases had leucocytosis. In CP, 6 (6.5%) cases presented with leucopenia, 68 (73.9%) cases presented with leucocytosis and 18 (19.6%) cases presented with normal leucocyte count. In AP, 100% cases presented with leucocytosis. And in BC phase, 1 (33.3%) case presented with leucocytosis and 2 (10%) cases presented with normal leucocyte count (Figure 2).

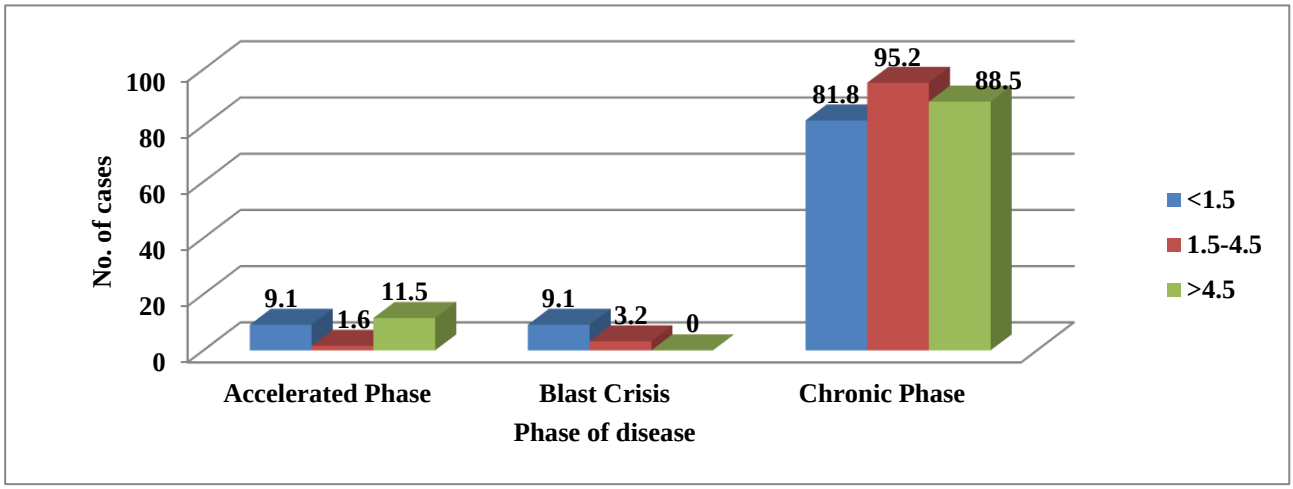

Figure 3: Platelet counts and different phases of disease.

Table 2: Correlation between different parameters of disease.

		Spleen size	TLC	Basophils	Platelets	Hb
Spleen size	Pearson correlation	1	0.211	0.041	-0.067	-0.121
	Sig. (2-tailed)		0.036	0.687	0.507	0.231
	N	100	100	100	100	100
TLC	Pearson correlation	0.211	1	0.098	0.198	-0.103
	Sig. (2-tailed)	0.036		0.330	0.048	0.310
	N	100	100	100	100	100
Basophils	Pearson correlation	0.041	0.098	1	0.087	-0.244
	Sig. (2-tailed)	0.687	0.330		0.390	0.015
	N	100	100	100	100	100
Platelets	Pearson correlation	-0.067	0.198	0.087	1	0.112
	Sig. (2-tailed)	0.507	0.048	0.390		0.266
	N	100	100	100	100	100
Hb	Pearson correlation	-0.121	-0.103	-0.244	0.112	1
	Sig. (2-tailed)	0.231	0.310	0.015	0.266	
	N	100	100	100	100	100

Normal platelets count: 1.5-4.5 lakhs/cumm, thrombocytopenia: <1.5 lakhs/cumm, thrombocytosis: >4.5 lakhs/cumm

Out of total, 63% cases presented with normal platelet count, 11% cases presented with thrombocytopenia and 26% cases presented with thrombocytosis. Increased platelet count (>450×103/dl) was seen more in patients of CP (88.5%). Thrombocytopenia was noted more among patients of CP (81.8%) compared with other phases of CML (Figure 3).

There was a significant direct correlation between spleen size and WBC count (pearson's correlation=0.211; p= 0.036), and also a significant direct correlation between total leucocyte count and total platelet count (Pearson correlation=0.198; p=0.048). Similarly, basophils percentage in peripheral blood had significant inverse correlation with haemoglobin levels (Pearson correlation=−0.244; p=0.015). There was insignificant relation between spleen size and platelet counts of patients (Table 2).

DISCUSSION

The present study was conducted on 100 patients of CML to obtain the demographic, clinical, haematological profile and risk stratification on the basis of EUTOS visiting to a single tertiary care hospital. Chronic myeloid leukaemia is diagnosed in all patients on the basis of bone marrow aspiration and biopsy and BCR-ABL by RT-PCR quantitative assay test. Most literature from the Western studies shows median age of presentation is 55 years (European) and 66 years (Americans). The median age of presentation in our study is 42 year. Thus, the age of diagnosis of CML in Indian population is a decade earlier from the Western population.[8] Median age in this study was 42 years, which was comparable with Deshmukh et al where median age of presentation is 38 years.[9] The male:female ratio of CML patients in our study was 1:1

but male preponderance was seen in all the Indian as well as all international studies. In the study conducted by Khaled et al an overall 57.2% of them were female, with a male-to-female ratio of 1:1.7.[16]

The majority of patients (92%) were in CP stage and in AP and BC phase patients presented are 5% and 3% respectively. Ahmed et also reported that frequency of all three phases of CML to be 77.8%, 15.5%, and 6.7%, respectively, were observed in among the 45 patients suffering from CML.[10] Tardieu et al study in France reported the frequencies of CP, AP, and BC as 96.8%, 2.2%, and 0.9%, respectively.[11] More patients in CP phase in our study as well as in neighbouring countries may be explained as the patients may present at early stage of the disease.

Splenomegaly was seen in 64% cases which was same as in Western countries and was in contrast to Indian scenario as see in Ganeshan et al study.[12] In our study mild, moderate and massive splenomegaly seen in 26%, 16% and 22% cases respectively which is in contrast to the study conducted by Sandeep Kumar et al which showed massive splenomegaly in 62.2% cases, moderate splenomegaly in 22.2% cases, and mild splenomegaly in 15.6% cases.[13]

In our study, mean value of total leucocyte count is 155×103/µl and it was 182.5×103/µl in study conducted by Sandeep et al.[13]

Mean hemoglobin was 9.44±2 g/dl with median value 9.45 g/dl. Sandeep Kumar et al. found mean hemoglobin was 9.41±1.75 g/dl with median value 9.5 g/dl in CML patients. In this study, anemia was seen in 90% which was similar to studies conducted by Sandeep Kumar et al and Singh et al.[13,14] In our study, majority (51%) were suffering from moderate anemia. Chang et al also found moderate anemia in 46.9% in CML patients.[15]

Hepatomegaly was seen in 45% cases, which was not compareable with study conducted by Khaled et al in Egypt and Chang et al in Aligarh as in them hepatomegaly was seen in 76% and 18% cases respectively.[15,16]

In our study majority (63%) of patients presented with normal platelets count and 11% cases with thrombocytopenia and 26% cases with thrombocytosis which is comparable to the study conducted by Sandeep et al. which shows 68.9%, 6.7% and 24.4% cases with normal platelet count, thrombocytopenia and thrombocytosis respectively.

Chronic phase of CML

In our study, 92% of the patients were in CP. Among the patients in CP, 45 (48%) were males and 47 (51%) were females. The male to female ratio was 0.9:1 which is not comparable with the other Indian and International studies. Most of the patients of CP had anemia (90%). Most of the patients had hemoglobin in the range 7-10 g/dl (47%) followed by mild anemia (>10 g/dl) seen in 26% of cases. This is similar to study conducted by Sandeep Kumar et al most of the patients had leucocytosis (68%). Most of the patients had normal platelet counts (60%).

These findings are similar to study by Sandep Kumar et al who found Most of the patients had leucocytosis (52.2%) and most of the patients had normal platelet counts in the range (68.9%). In CP, 23% had thrombocytosis. This finding is similar to study by Bhatti et al who found thrombocytosis in 26% of the cases in CP.[17]

Accelerated phase of CML

In our study, 5% of the patients were in AP. Among the patients in AP, 2 (40%) were males and 3 (60%) were females. All the patients had anaemia (100%). These findings are against to Bhatti et al study which showed 96% cases had anaemia. All patients had leucocytosis (100%). This finding is against to Sandeep Kumar et al study which showed leucocytosis only in 63.6% cases. Majority of the patients had thrombocytosis which is comparable to the study of Bhatti et al that thrombocytosis was seen maximum in patients of AP.[17]

Blast crisis phase

About 3% of the patients were in BC and all were males. 33.3% cases had thrombocytopenia, 33.3% cases had leucocytosis and 66.6% cases had anaemia. These all findings are against to the studies conducted by Bhatti et al and Kumar et al.[13,17]

Despite being common malignancy in India, literature search does not show any study from this part of country which few studies seen from areas, such as Gujarat, Haryana, Assam, northern Karnataka, Delhi, Mumbai, Calcutta, Uttar Pradesh etc. but not in this geographical area.

CONCLUSION

Therefore, to conclude, most CML patients in north west Punjab are relatively young (31-40 years) with male:female ratio is 1:1. Most of them belongs to Sikh religion and rural residency. Most of them presented in chronic phase of the disease and with low risk strata according to EUTOS. Mean size of the spleen on presentation was 15.6±4.2 and mean haemoglobin level was 9.4±2. Means most patients presents in early phase of disease, with anaemia, leucocytosis or splenomegaly.

ACKNOWLEDGEMENTS

First of all, I thank God Almighty and my parents Mr. Satnam Singh and Mrs. Rani Kaur, my brother

Harmandeep Singh who supported me with love and understanding. Without them, I could never have reached this current level of success.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kaur R, Gupta R, Chandey M, Singh P, Mohan G, Singh N. Study of demographic, hematological profile and risk stratification in chronic myeloid leukemia patients, in and around North-West Punjab, India. Int J Adv Med 2020;7:1789-94.